EMERGING DISEASE INSIGHTS

Research from the PREDICT Modeling & Analytics team

Preliminary Analysis of Geographic Distribution, and Host and Vector Range for Understudied Flaviviruses

The ongoing Zika virus was declared a public health emergency of international concern by WHO in February 2016, due to its rapid spread and detrimental birth defects. Despite discovery in 1947, evidence of human infection, and being closely related to high-impact human viruses like Dengue and Yellow Fever, the study of Zika remained limited until the Yap Island outbreak 2007[1] (Figure 1). The pandemic spread of Zika emphasizes the need to better understand the distribution, host range, and epidemic potential of other understudied Flaviviruses[2].

The PREDICT-2 Modeling & Analytics team compiled a database of all known natural host and vector species for 53 ICTV-recognized viruses[3] in the genus Flavivirus. In total, 1768 flavivirus-host associations (including 317 unique mammal species and 743 bird species) and 309 flavivirus-vector associations (149 unique insect vector species) were identified. We then calculated the taxonomic breadth and geographic range of each flavivirus in order to inform both current and potential risk of flavivirus spillover and spread.

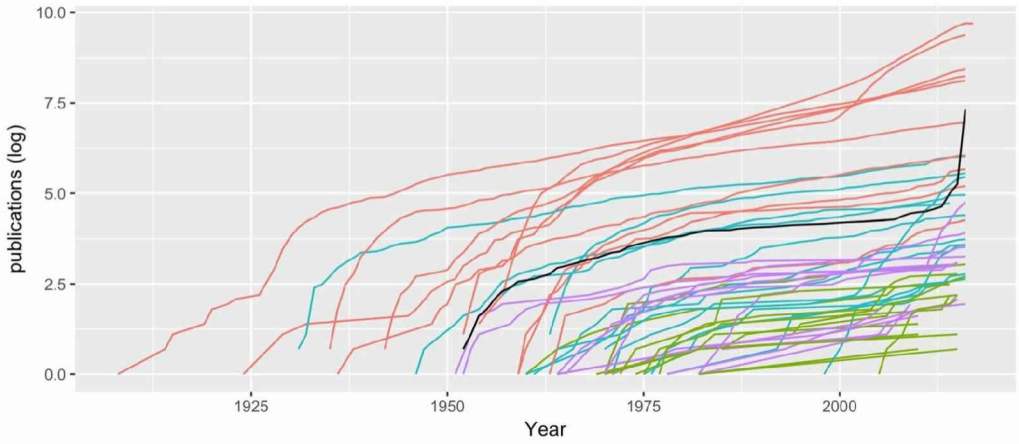

Figure 1: Publication effort 1900-2016 of each Flavivirus (n = 53). Publication counts retrieved from Web of Science on 10/27/16. Line color based on level of human impact: epidemic viruses (>20 pathogenic cases) in red, rare viruses (<20 pathogenic cases) in teal, subclinical viruses (detected only via serology) in purple, nonhuman viruses in green. Zika is colored black to emphasize the sharp rise in publications after its human impact changed to epidemic in 2007.

In order to control for the effect of research effort, and understand the relative importance of host and vector breadth in the zoonotic potential of Flaviviruses, we developed a generalized linear model of likelihood a virus is zoonotic. We simplify host and vector breadth to the lowest taxonomic group that encompasses all known natural host or vector species. Both non-human host breadth ($p = 0.02$) and vector breadth ($p = 0.03$) were significant in modeling zoonotic status of virus, so these variables were used to rank viruses by emergence potential (Table 1). Using the IUCN mammalian range and BirdLife spatial files, we created a unique vertebrate host distribution layer for each flavivirus, and combine these to produce a global map of known

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flaviviruses diversity in wild mammals and birds (Figure 2).

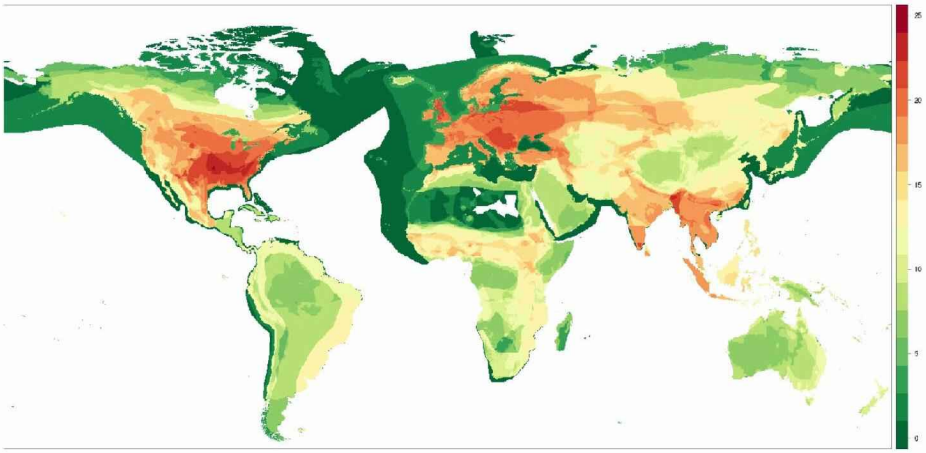

Figure 2:. Geographic map of currently known Flavivirus diversity in wild mammals and birds (n = 42 viruses). Virus distribution calculated as aggregate range of all mammal and bird hosts for each virus (1 to 294 host per virus, median = 3). Redder regions show higher concentration of unique Flaviviruses based on vertebrate host range.

Of the 53 Flaviviruses, 37 (70%) have been detected in humans, and 25 of these human-associated flaviviruses have yet to cause significant outbreaks. Using taxonomic breadth of host and vectors, we prioritize these 25 pre-epidemic flaviviruses for futher research using just two variables (host and vector breadth) that relate to zoonotic and epidemic potential (Table 1).

Table 2: The top 10 pre-epidemic human flaviviruses based on large host and vector breadth. Current human infection is classified as subclinical (only detected in humans via serology) or rare (<20 human cases).

Virus	Human Infection	Host Bread	Vector Breadth	Host Orders
Wesselsbron virus	rare	Phylum	Phylum	4
Usutu virus	rare	Phylum	Family	11
Ilheus virus	rare	Phylum	Family	4
Louping Ill virus	rare	Phylum	Genus	8
Uganda S virus	subclinical	Phylum	Genus	2
Tembusu virus	subclinical	Class	Family	3
Aroa virus	rare	Class	Family	2
Bagaza virus	rare	Class	Family	2
Saboya virus	subclinical	Class	Species	5
Apoi virus	rare	Order	none	1

As Zika and other flaviviruses continue to spread from once constricted geographic areas through increased human travel to new environments, the natural host range will be of critical importance in determining risk of viral spillover and spread. Zika virus has now been detected in South American mammals[4], which shows that human transport of a virus can lead to establishment in new animal hosts, potentially leading to new sylvatic cycles and endemicity.

Additional coming analyses of these host, vector, and geographic range data for neglected flaviviruses are underway to better inform the likelihood of spillover and global spread.

References

1. Kindhauser, M. K. *et al.* Zika: the origin and spread of a mosquito-borne virus. Bull World Health Organ 171082 (2016).
2. Olival, K. J. & Willoughby, A. R. Prioritizing the dormant flaviviruses. EcoHealth (2017).
3. King, A. M. *et al.* Virus taxonomy: classification and nomenclature of viruses: Ninth Report of the International Committee on Taxonomy of Viruses. Vol. 9, Elsevier (2011).
4. Favoretto, S. *et al.* First detection of Zika virus in neotropical primates in Brazil: a possible new reservoir. bioRxiv, 049395 (2016).